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SYMPOSIUM ON CHEMICAL APPLICATIONS OF TOPOLOGY AND GRAPH THEORY

Georgia Center for Continuing Education

University of Georgia

Athens, Georgia 30602, U.S.A.

April 18-22, 1983

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Collected short abstracts of papers

SYMPOSIUM ON CHEMICAL APPLICATIONS OF TOPOLOGY AND GRAPH THEORY

PROGRAM

Monday, April 18, 1983

R. B. King, presiding
9:00 AM   Opening remarks

Dr. Robert C. Anderson, Vice-President for Research, University of Georgia
and President, University of Georgia Research Foundation
Dr. W. J. Payne, Dean, College of Arts and Sciences, University of Georgia

9:30 AM   J. Dugundji, "Qualitative Stereochemistry"

10:30 AM   Coffee Break

*11:00 AM   O. Sinanoğlu, "Algebraic and Topological Structure of Quantum Chemistry
and of Chemical Kinetics"

12:00(noon) P.J. Plath and E. C. Hass, "Logic of Chemical Ideas"

12:30 PM   Lunch, Georgia Center for Continuing Education

W. C. Herndon, presiding
2:00 PM   R.E. Merrifield and H. E. Simmons, "Finite Point-Set Topology and Molecular
Structure"

3:00 PM   R. F. W. Bader, "A Theory of Molecular Structure"

4:00 PM   Break

4:30 PM   P. G. Mezey, "Reaction Topology: Manifold Theory of Potential Surfaces
and Quantum Chemical Synthesis Design"

5:30 PM   Adjourn for dinner

7:30 PM   Wine and Cheese Party, Taylor-Grady House, Prince Avenue, Athens, Ga.

Tuesday, April 19, 1983

E. Wegman, presiding
8:30 AM   F. Harary, "Some Graph Theoretic Models in Theoretical Chemistry"

9:30 AM   K. Balasubramanian, "Symmetry and Spectra of Graphs and their Chemical
Applications"

10:00 AM   Break

10:30 AM   M. Randić, "On Ordering of Graphs and Structures and their Properties"

11:30 AM   A. C. Day, R. B. Mallion, and M. J. Rigby, "On the Use of Riemannian Surfaces
in the Graph-Theoretical Representation of Möbius Systems"

12:00(noon) D. M. Walba, "Stereochemical Topology"

12:30 PM   Lunch, Georgia Center for Continuing Education

D. Nelson, presiding
2:00 PM   W. C. Herndon, "Canonical Labeling and Isomorphism of Graphs: Applications
           to Descriptors of Chemical Compounds"

*3:00 PM   M. Barysz, G. Jashar, R. S. Lall, V. K. Srivastava, and N. Trinajstić, "On
           the Distance Matrix of Molecules Containing Heteroatoms"

3:30 PM   Break

4:00 PM   D. H. Rouvray, "Should We Have Designs on Topological Indices?"

5:00 PM   V. R. Magnuson, D. K. Harriss, and S. C. Basak, "Topological Indices Based
           on Neighborhood Symmetry: Chemical and Biological Implications"

5:30 PM   Adjourn

Wednesday, April 20, 1983

C. Holland, presiding
8:30 AM   H. G. Othmer, "The Global Dynamics of Certain Classes of Reaction Networks"

9:30 AM   R. Thomas, "Logical versus Continuous Description of Systems Comprising
           Feedback Loops"

10:30 AM   Break

11:00 AM   B. L. Clarke, "Qualitative Dynamics and Stability of Chemical Reaction
           Networks"

12:00(noon) Lunch, Georgia Center for Continuing Education

R. B. King, presiding
1:30 PM   O. E. Rössler and J. L. Hudson, "Higher Chaos in Simple Reaction Systems"

2:30 PM   R. Larter, "The Use of Sensitivity Analysis in Determining the Structural
           Stability of Multi-parameter Oscillators"

3:00 PM   Break

*3:30 PM   H. Degn, "Periodic Perturbations of Next Period Functions"

4:00 PM   L. Peusner, "Electrical Network Representations of n-Dimensional Chemical
           Manifolds"

4:30 PM   C. Trindle and R. Givan, "A LISP Program for the Manipulation of Chemical
           Graphs"
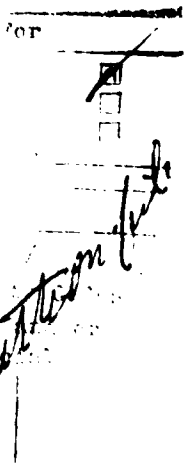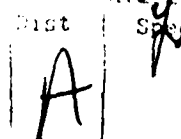
5:00 PM   Adjourn technical sessions for the day

7:00 PM   Symposium barbecue, Pinecrest Lodge

Thursday, April 21, 1983

E. Wegman, presiding
8:30 AM   E. C. Hass and P. J. Plath, "The Multi-Dimensional λ-Model. A Graph
           Theoretical/Algebraic Approach to Describe Mechanistic Aspects of Complex
           Chemical Reactions"

9:00 AM   P. H. Sellers, "The Classification of Chemical Mechanisms from a Geometric
           Viewpoint"

9:30 AM   S. H. Bertz, "The Modeling Molecular Complexity"

10:00 AM   G. A. Jones and E. K. Lloyd, "The Automorphism Groups of Some Chemical
           Graphs"

10:30 AM   Break

11:00 AM   D. J. Klein and W. A. Seitz, "Graphs, Polymer Models, and Excluded Volume
           Effects"

12:00(noon) L. V. Quintas, "A Volume Function for Water Based on a Random Lattice-
           Subgraph Model"

12:30 PM   Lunch, Georgia Center for Continuing Education

D. Nelson, presiding
2:00 PM   R. B. King, "The Bonding Topology of Polyhedral Molecules"

3:00 PM   A. G. Turner, "Topological Properties of Sulfur Nitrogen Compounds"

3:30 PM   M. J. McGlinchey and Y. Tal, "The Shapes of Main Group Clusters: A Topological
           Approach to Skeletal Electron Counting"

4:00 PM   Break

4:30 PM   H. M. Martinez, "Dynamics of RNA Secondary Structure Formation"

5:00 PM   S. Swaminathan, "Topological Aspects of Enzyme-Substrate Recognition"

5:30 PM   Adjourn for dinner

Friday, April 22, 1983

R. B. King, presiding
9:00 AM   Informal discussion on Future Directions for Research on Chemical Applications
           of Topology and Graph Theory

11:00 AM   End of Symposium

*)Abstract not available in time to include in this collection.

QUALITATIVE STEREOCHEMISTRY

J. Dugundji

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The outline of a unified treatment of Stereochemistry, applicable
to all molecules, flexible or not, will be presented. It is based on
joint work with Ugi/Marquarding/Kopp, expressing the viewpoint that
Stereochemistry cannot be treated adequately by considering the
molecular geometry separately from the molecular chemistry; it is the
interaction of these two features that is fundamental. This interaction
is shown to be expressible by a group, called the chemical identity
group of the molecule. Various stereochemical phenomena are described
directly by this group and its properties. For example, the number of
chemically distinct isomers in a family of permutation isomers can be
determined and representatives of those isomers exhibited; chirality
phenomena can be explained and predicted; the notion of an isomerization
can be formulated precisely, and the possible intermediates or
mechanisms can be determined.

The approach does not use energy considerations, being qualitative
in the sense that all the theoretically possible outcomes of a
stereochemical experiment are determined, thereby narrowing the
possibilites deserving further experimental consideration.

Abstract

L O G I C   O F   C H E M I C A L   I D E A S

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Based on the graph-theoretical formulation of several mechanisms, which
might be possible using chemical structure theory, the applied chemical
ideas have been analyzed logically. To illustrate our analysis we take
examples of rearrangements within transition states of carbo-cations,
as we can observe in the Demjanov-rearrangement as well as in acid-cata-
lysed isomerisations within zeolite cavities. It can be shown that the
declaration of any chosen mechanisms destroy the holistic character of
an unprejudied description of the whole reaction.
The orthomodular lattice of pr positions concerning the holistic descrip-
tion of the reaction has to be reduced to a boolean sublattice by de-
claring one of the mechanisms.

It can be shown that different conceptions on the molecular structure
of carbo-cations corresponds with the introduction of special pre-
assumptions, which cut out the boolean sublattice out of the reaction
lattice.
Introducing a norm on such a boolean lattice one get the possibility for
probabilistic interpretation within the scope of the chosen presupposition.

Key-words:

Lattice-theoretical investigation of chemical reaction mechanism;
graph-theoretical description of chemical formulae.

FINITE POINT-SET TOPOLOGY AND MOLECULAR STRUCTURE

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A topological description of molecular structure has been
developed which derives from the one-to-one correspondence between
transitive digraphs on $\underline{n}$ vertices and finite topologies on $\underline{n}$ points.
The two possible transitive orientations of a bipartite graph lead to a
unique topology-cotopology pair associated with any alternant molecule.
A similar pair of spaces is associated with a nonalternant (whose graph
may have many or no transitive orientations) via its duplex, which is
the graphical conjunction with K_2 and is necessarily connected and
the only homeomorphic spaces are those of stereoisomers. The structure
of these molecular spaces can be analyzed quantitatively by a variety of
combinatorial measures. The cardinality of the molecular topology is
a measure of structural complexity which increases with branching and
decreases with cyclization. A topological correlate of delocalization
in π-electron systems is the degree to which an atom or adjacent pair of
atoms approximates a disconnected subspace of the molecular space. The
patterns of free valences and π-bond orders given by this measure are in
excellent agreement with molecular orbital theory.

A THEORY OF MOLECULAR STRUCTURE

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A theory of molecular structure has been developed which demonstrates that the concepts of atoms and bonds may be rigorously defined in terms of the topological properties of the observable distribution of charge for a molecular system. As a consequence of these definitions, one in turn obtains a definition of structure and a predictive theory of structural stability. The theory is linked to quantum mechanics by demonstrating that the atoms so defined represent a class of open quantum subsystems with a unique set of variationally defined properties. The definition of structure associates a given structure with an open neighbourhood of the most probable nuclear geometry, and removes the need to invoke the Born-Oppenheimer approximation for the justification or rationalization of structure in a molecular system. By defining all possible structures for a given system, the theory shows that a change in structure must be an abrupt and discontinuous process, one which is describable in terms of the mathematical theory of dynamical systems and their stabilities.

The application of the notion of structural stability to the topological study of the molecular charge distribution leads to a partitioning of the nuclear configuration space into a finite number, ℓ, of non-overlapping regions, the structural regions $W_i (i=1,\ldots,\ell)$, each of which is characterized by a unique molecular structure. These structural regions form a dense open subset of the nuclear configuration space. A point which belongs to the union of the W_i belongs to some structural region, and is called a regular point. A nuclear configuration belonging to the complementary of the set of regular points is called a catastrophe point. The catastrophe set is the union of the boundaries of all the ℓ structural regions W_i.

We distinguish two types of catastrophe points. This distinction arises as a corollary of a theorem on structural stability first stated by Palis and Smale. The immediate consequence of the theorem is that a structural instability can be established through either of two mechanisms: in the bifurcation mechanism the charge distribution exhibits a degenerate critical point, while the conflict mechanism is characterized by the non-transversal intersection of the stable and unstable manifolds of pairs of critical points in the charge density. Catastrophe theory may be used to provide a mathematical model for structural changes in the neighbourhood of a bifurcation point, through the analysis of the universal unfoldings associated with singularities of particular kinds.

REACTION TOPOLOGY: MANIFOLD THEORY OF POTENTIAL SURFACES AND QUANTUM CHEMICAL
SYNTHESIS DESIGN

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ABSTRACT

In the last decade the development of advanced quantum chemical methods and
the related applied mathematical techniques, as well as the spectacular improve-
ment of the available computer hardware and software, made quantum chemistry an
important complement of experimental chemical research. In the foreseeable
future it will be economically feasible to carry quantum chemical model studies
on a variety of possible synthetic pathways before the actual synthesis of a
new compound is attempted. Reaction topology and manifold theory of quantum
chemical potential energy hypersurfaces of reacting chemical systems are pro-
posed for the global and local analysis of the set of all reactions of all
molecules composed from a given set of N nuclei and k electrons.

The topological model of potential energy hypersurfaces leads to some
simplifications in the actual quantum chemical calculations. It forms a
rigorous quantum chemical basis for a topological definition of molecular
structure and reaction mechanism. Intersection graphs of topological open sets
of a manifold, replacing the concept of the conventional nuclear configuration
space, lead to a global quantum chemical reaction network model, which network
can be utilized in computer-aided synthesis planning.

SOME GRAPH THEORETIC MODELS IN THEORETICAL CHEMISTRY

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Abstract

The best known graph theoretic model in theoretical chemistry, and perhaps the first one, is the representation of a molecule M by the graph $G = G(M) = (V,E)$ in which the point set V of G is the collection of atoms in M, and two points of G are adjacent whenever the corresponding atoms of M have a chemical bond joining them. Of course G is permitted to be a multigraph to allow for multiple bonds joining two atoms as in an unsaturated hydrocarbon. This model has been most useful for the determination of the number of isomers of tree-like molecules and others; the original formulas by Cayley were extended by Pólya in a general enumeration theorem, simplified by Otter, and also studied by Balaban. However it required additional methods to resolve the enumeration of chiral and achiral alkenes. These methods used the Power Group Enumeration Theorem to count 2-dimensional achiral plane trees, and were easily modified to handle 3-dimensional achiral alkenes.

Although the phrase 'the topology of a molecule' M always means the graph of M, the present decade has seen the synthesis of molecules with graphs homeomorphic to both of the prototypical nonplanar graphs of Kuratowski: the toroidal graph K_5 and the smallest mobius ladder $K_{3,3}$, the latter constructed by Walba.

Another graph theoretical model involves the expression of chemical reactions in terms of two different graphs with the same degree sequence. This model motivated the chemist, Senior, to characterize for the first time those graphical degree sequences which belong to exactly one graph. The graphs known as polyhexes constitute the table of contents of the classical books on organic chemistry by Clar. The square-celled and triangular-celled animals have also been mentioned in the chemical literature.

The spectrum of a graph, consisting of the nonincreasing sequence of the (real) eigenvalues of its adjacency matrix has a genuine chemical signifi-

cance. However the spectrum does not uniquely determine the graph of the molecule, contrary to chemical rumors which had been widely circulated. Spectral considerations also do not settle the celebrated Reconstruction Conjecture of graph theory although this assertion has been claimed in the chemical literature. The matching polynomial of a graph has been utilized by the Yugoslav chemist, Gutman, leading to a joint paper which generalized it, using line graphs. Finally, electronegativity considerations tell the strength of a chemical bond, suggesting undirected networks as a numerical rather than strictly topological model.

Symmetry and Spectra of Graphs and Their Chemical Applications

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The use of pruning methods and other graph product
methods for the symmetry and spectra of graphs will be
outlined. It will be shown that symmetry groups of
several graphs of chemical interest can be expressed
as generalized wreath product groups. Applications of
these methods to dynamic NMR spectroscopy of non-rigid
molecules will be considered. Spectra of weighted
trees will be obtained using a tree-pruning method.
These methods will be applied to NMR spectroscopy and
chemical kinetics since graphs with weighted couplings
(coupling constants in the case of NMR) play an
important role in these areas.

M. Randić [a], G. Kraus [b] and B. Džonova Jermon-Blažic [c]

Ordering of Graphs as an Approach to Structure-Activity Relationships

We consider molecular graphs which are represented by sequences $(p_1, p_2, p_3 \ldots p_4)$, where p_i counts the number of paths (self-avoiding walks) of length i. The path numbers p_i are constructed in a novel way (without a use of a computer) suitable when family of structures having different substituent are considered. In particular we consider a number of derivatives of phenanthrene carbinol, including a few structures reported in the literature as illustrations of "compounds that don't fit" the widely used QSAR approach of Hansh, which is essentially a multiparametric regression scheme using empirical parameters. The compounds are showing variable degree of antimalarial activity. As a consequence of the established partial order among the structures when the most potent autimalarials are taken as standards we were able to make predictions on the most likely derivatives of phenanthrene carbinol which may be expected to exhibit high antimalarial potency. Synthetic work is in progress on one such compound.

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ON THE USE OF RIEMANNIAN SURFACES IN THE GRAPH-THEORETICAL REPRESENTATION OF MÖBIUS SYSTEMS

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ABSTRACT

Möbius systems have been studied by a novel graph-theoretical method involving non-planar graphs that may be embedded without crossing on a two-sheeted Riemannian surface. In this formulation, negative entries in the resulting adjacency-matrices arise quite naturally from the mathematics of the Riemannian surfaces, without the necessity of recourse to more-intuitive physical considerations. It is further emphasised that the provisions of the Perron-Frobenius theorem on non-negative matrices do not apply to the adjacency matrices of Möbius graphs, and the consequences of this fact for the eigenvalues and eigenvectors of such graphs are discussed.

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* Presenter of the paper.

STEREOCHEMICAL TOPOLOGY

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In 1961 Edel Wasserman coined the term chemical topology to describe certain novel isomerisms which may occur in macrocyclization processes. Chemists thus began consideration of the topology of molecular structures in the context of stereochemistry. We consider the bond graph as the construction composed of the nuclei (points) with adjacency determined by whether the atoms are considered bonded or not. Adjacency is thus arbitrary to some extent. However, for most molecules, construction of such a molecular bond graph is straightforward. Stereochemical topology deals with extrinsic properties of this bond graph deriving from embedding in three-space. We define stereochemical topology as the synthesis and characterization of stereoisomers which are toplogically distinct in three-dimensional space. Such novel constructs as catenated rings, knotted rings, and molecular Möbius strips belong in the realm of stereochemical topology. We have recently developed efficient methodology for construction of molecular ladders composed of two polyether chains connected by double bonds. The chains are functionalized such that they may be connected end to end, thus generating cylindrical products. When the number of rungs in the starting molecular ladder is three or more, the products formed upon macrocyclization are homeomorphic with either prisms, or Möbius ladders. (Möbius ladders are graphs defined by Harary and Guy.) Becuase of the embedding in three space, unique molecular cylinders (prisms) with n vertecies may, of course, possess either zero or an even number of $\frac{1}{2}$ twists, while the molecular Möbius ladders possess an odd number of $\frac{1}{2}$ twists. By cleavage of the double bonds of these novel molecules, molecular knotted rings and linked rings, including multiply looped catenanes, may be prepared. Discussion will focus on the novel topological properties of these products, and on general criteria for toplogical enantiomerism and diastereoisomerism. Topological enantiomers must be non-planar, either defining a non-planar graph (the Möbius ladder with six vertecies is homeomorphic with $K_{3,3}$) or a knot or link which is non-planar by virtue of it's embedding. In addition, there may be no presentation with an imporper axis of symmetry. Interestingly, these criteria are necessary, but not sufficient for toplogical chirality. For toplogical diastereoisomerism, at least one of the isomers must be non-planar.

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Graph theoretical characterizations of molecular graphs can be used for two principal purposes.   One is to provide an alphanumeric description or code to aid in the processing or retrieval of chemical structures.   It is desirable to have a unique code for any given molecular structure (including stereochemistry), and this requirement is related to problems of graph isomorphism for which many solutions have been proposed. A unique labelling of a molecular graph gives a solution for the unique coding problem. Following the work of several previous investigator, we have recently proposed a method for uniquely denoting polynuclear cluster compounds.   The method begins with an algorithm for canonically numbering the molecular graph, and then converts this numbering into a compact linear form of a complete labeled adjacency matrix.   The algorithm uses the concept of extended connectivity and a perturbation method to lable the graph.   The explicit ordering of the final listing completely specifies stereochemical configuration at stereo-centers in the cluster.   The procedure is easily carried out hand, and if two molecular graphs have identical notations isomorphism is established.   The canonical labelling procedure has been extended to several graphs which are highly resistant to many other canonical numbering methods.

Graph theoretical properties of molecular graphs also give rise to numerical indices derived from the structure which can be used for correlation with physical or chemical properties.   This is a well-known and worthwhile application of graph theory to chemistry with many reported successful correlations.   Many of these topological indices have also been proposed to be useful in solving graph isomorphism questions, especially when several indices are combined into a single "super-index".   However, no combination of topological indices can be shown to be sufficient to establish isomorphism and a canonical labelling procedure would seem to be a more useful approach to questions of this type.

SHOULD WE HAVE DESIGNS ON TOPOLOGICAL INDICES?

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Over the past three decades it has become increasingly clear that many of the physicochemical properties of substances are determined primarily by the underlying topological structure of the molecular species of which they are constituted. The topological structure of a given species can be formulated in mathematical terms by means of a topological index which reflects not the metric properties of the species but rather its overall shape and size. To date, some 20 different topological indices have been devised and correlations with physicochemical parameters have been obtained for most of them. Although differing indices vary in their sensitivity to characterize molecular branching, the correlations found for a wide range of parameters have, in general, been good to excellent. Topological indices can thus now be regarded as a valuable predictive tool for chemists and others.

After tracing their early historical evolution, we enumerate here all of the major topological indices which have been postulated so far. The mathematical relationships known to exist between various indices are also exhibited and it is concluded that virtually all of the indices are inter-related. The manifold new areas of potential application of such indices in the future are explored under three main headings: bibliographical species classification, physicochemical parameter evaluation and pharmaceutical drug design. It is pointed out that the indices are likely to become increasingly important for the prediction of species behavior in both inanimate and living systems. Novel pharmaceutical and medical applications in particular appear to warrant further study. The question posed in the title of the paper can thus be answered in the affirmative: designs on the utilization and exploitation of topological indices in several as yet uncharted domains are certainly admissible.

TOPOLOGICAL INDICES BASED ON NEIGHBORHOOD SYMMETRY: CHEMICAL AND BIOLOGICAL APPLICATIONS

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One of the current trends in chemistry and molecular pharmacology is the progressive use of topological molecular descriptors in the correlation of physicochemical and biological properties of molecules. One of the more interesting approaches in this area is the development of information-theoretic invariants. The essence of the approach is to partition the appropriate set of elements derived from the molecular graph into disjoint subsets on the basis of a selected equivalence relation, construct a probability scheme and calculate the structural complexity (information content) using Shannon's formula.

Like atoms in a molecule may possess quite different physical and chemical characteristics depending upon the number and nature of their neighbors. To account for this phenomenon, we have developed a formalism where the equivalence relation is constructed to partition the atom set according to their zero, first and higher order neighbors in the total molecular graph. For a vertex v in the graph G, an open sphere, $S(v,r)$, is defined as

$$S(v,r) = \{u: d(u,v) < r\} \tag{1}$$

where r is any non-negative real number. $S(v, e+1)$ can be expressed as the union of the disjoint neighbors $\tau^i(v)$, $(i=0,1,\ldots,e)$, where e is the eccentricity of the vertex v. One can then construct all such open spheres, $S(v,r)$, where v runs over the entire vertex set $V(G)$ and these form a neighborhood system for the vertices of G. An equivalence relation is then defined to achieve zero, first and higher order partitioning of $V(G)$. Subsequently, Shannon's formula is used to calculate the various order information contents (IC_v) of the graph.

The utility of IC_v and other derived indices is demonstrated by correlating these molecular descriptors with the aqueous solubility of 51 alkanols and the narcotic action of a group of thirteen barbiturates. The relative efficacy of these newly formulated indices _vis-a-vis_ other topological indices, viz., Wiener number (W), molecular connectivity ($^1\chi$, $^1\chi^v$), information indices on the distance matrix (I_D^W, I_D^{W}), and partition coefficient (log P, octanol-water) is also analyzed for barbiturate narcosis.

THE GLOBAL DYNAMICS OF CERTAIN CLASSES

OF REACTION NETWORKS

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One aspect of chemical kinetics concerns the prediction of the
qualitative dynamics of a reacting mixture based on information about
the topology of the reaction network and the dependence of the rates on
the concentration of the various species. A graph-theoretic approach is
natural for such problems because it leads to a factorization of the
equations of change in which the effects of stoichiometry, network
structure and reaction rate phenomenology can be studied separately.
This in turn leads to a classification of the steady states and an algorithm
for systematically determining which, if any, of the various types exist in
a given network. This approach also leads to a complete description of the
global dynamics of a subset of what are called vertex-controlled networks.
In particular, one can show that the equations for such networks always have
exactly one steady state that is globally-asymptotically stable, and if such
networks are periodically-forced, the system always relaxes to a periodic
solution with period equal to that of the driving function.

LOGICAL vs CONTINUOUS DESCRIPTION OF SYSTEMS COMPRISING FEEDBACK LOOPS

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Looped systems comprising multiple non linear interactions can be described in terms of differential equations, as used for instance in chemical kinetics. However, unless the number of variables is very low these systems cannot be treated analytically, and such essential qualitative properties as the number and quality of the attractors have often to be ascertained from numerical identification of steady states, for more or less arbitrary chosen values of the parameters.

The usefulness of a _logical_ description, i.e. a description in which variables can take only a limited number of values (usually two), has been realized for many years, and solutions proposed (see Rashevsky, 1954 ; Sugita, 1963 ; Kauffman, 1969 ; Glass, 1975). A method called since "Kinetic Logic" has been introduced some ten years ago (Thomas, 1973 ; Thomas and Van Ham, 1974). Its characteristic features are as follows :

1. To each relevant constituent (i) of a system we associate _two_ logical elements : a logical variable (α_i) describing the concentration (or more generally the _presence_ of the element, and a logical function (a_i) describing its rate of synthesis (or more generally, its _production_).

2. Time is not discretized. Rather, we associate with each couple (α_i, a_i) two (occasionally more) time delays ; switching on the function $(a_i=1)$ normally results in the appearance of the product $(\alpha_i=1)$ after a characteristic delay t_{α_i} and switching off the function $(a_i=0)$ normally results in the disappearance of the product $(\alpha_i=0)$ after a characteristic time delay $t_{\bar{\alpha}_i}$. This ensures a _fully asynchronous_, yeat perfectly practicable, treatment.

3. Each system is described by a set of _logical equations_ of the form $a_1 = f_1 (\alpha_1, \alpha_2, \ldots, \alpha_i, \ldots \alpha_n)$, a description which permits self input. The set of equations generates a _state table_ which gives the values of the logical functions for each set of values of the logical variables. From the state table one can generate a _graph of the sequences of states_ which permits the identification of the attractors (stable, periodic, ...) and the pathways towards them.

4. The conditions which impose the various pathways can be studied
   "analytically", this is without any prior assignement of numerical values
   to the time delays. In particular, one can perform a <u>logical stability
   analysis</u> of cyclic pathways.

   A recent description of this method can be found in Thomas (1983).

   In this talk I plan to discuss various aspects of the relation between my
logical equations and differential equations using sigmoid interactions
(as proposed e.g. by Goodwin (1965) and by Glass and Kauffman (1972))
In particular, we will see :

1. How one can infer from the logical description of a system the number and
   nature (stable steady states, limit cycles, ...) of the attractors of a
   homologous differential system (using sigmoid interactions).

2. How one can reverse the logical procedure so as to use it in an <u>inductive</u>
   way (instead of deducing the possible behaviours from the structure,
   we build a structure, as simple as possible, which will display a desired
   behaviour)

3. (A more recent development).
   How one can relate the parameters of the continuous description to the
   delays of the logical description.

QUALITATIVE DYNAMICS AND STABILITY OF CHEMICAL REACTION NETWORKS

Bruce L Clarke

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This paper presents concepts and computer alorithms that should enable a beginner to discover the qualitative dynamics of an ordinary reaction network. The algorithms supplied will run on an IBM personal computer. The paper begins with the practical aspects of setting up a network that faithfully represents that dynamics of a system on the time-scale of interest. Then it carries the reader through the analysis of a typical network and examines various theoretical questions of relevance along the way. A major topic is the structure of the manifold(s) of steady states, for these bear on the question of the existence of multiple steady states, the possibility of explosions and other exotic dynamics. The question of whether the steady states are globally attracting is treated using Lyapunov functions. Networks that have simple Lyapunov function are easily identified by tests that can be made by the computer algorithms supplied. The paper goes on to discuss how network structure can cause a breakdown of a simple type of qualitative dynamics and lead to more exotic dynamics. The latter part of the paper treats a number of questions: the effect of cycle length on instability, Lyapunov functions that can show that networks with exotic dyamics have their trajectories confined within a finite volume of dynamical space, and how the structure of networks can produce chaotic dynamics, and evolution.

Higher Chaos in Abstract Kinetics

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Abstract

Bifurcation parameters that are turned into slow variables by making them
dependent on one of the variables of the system provide a powerful means to
generate nontrivial higher-dimensional behavior [1]. For example, letting a
2-variable subsystem go through a Hopf bifurcation, via a slow third variable
coupled to one of the 2 variables, easily generates chaos (especially so if the
Hopf bifurcation leads to a large-amplitude limit cycle soon) [2]. Analogously,
letting a 3-variable subsystem go through a chaos-generating bifurcation (or
bifurcation sequence, respectively), via a slow fourth variable coupled to
one of the 3 variables, easily generates higher chaos (especially so if the
bifurcation leads to a large change in amplitude). And so on. As an example,
consider the following abstract reaction scheme:

Here A, B is the well-known Turing oscillator [3].
The addition of the (during part of its operation)
slow variable C leads to chaos (cf. [2]). The ad-
dition of the further slow variable D leads to
higher chaos. Note that the whole system (A+B+C+D)
is a simplified version of the Belousov-Zhabotinsky
reaction [4,5].
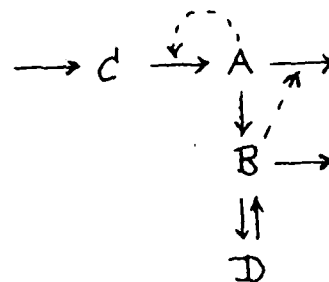
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THE USE OF SENSITIVITY ANALYSIS IN DETERMINING THE STRUCTURAL STABILITY
OF MULTI-PARAMETER OSCILLATORS

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ABSTRACT

   The use of sensitivity analysis for the study of models of oscillating reactions is
discussed. It is shown that linear sensitivity coefficients for oscillating systems almost
always contain secular terms; this makes a physical interpretation of the sensitivity
information very difficult. A new sensitivity method which eliminates the secular terms
via a uniformly valid expansion is derived. A method for extracting the modified
sensitivity coefficients from the ordinary sensitivity coefficients is proposed and
illustrated by application to the Lotka-Volterra oscillator.

ELECTRICAL NETWORK REPRESENTATION OF
n-DIMENSIONAL CHEMICAL MANIFOLDS

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A planar network representation, which utilizes lumped parameter elements
connected by Kirchhoff's laws, is used to represent the Riemmannian metric of
chemical energy manifolds. Thus, the consideration of primary concepts of
chemistry -- e.g., molecular structure, reaction mechanism, stability, etc. --
which can be analyzed by using quantum mechanical, kinetic, or thermodynamic
energy hypersurfaces reduces to the consideration of planar graphs. The input
currents in the network correspond to the contravariant components of the tangent
vectors in the directions of the manifold coordinates at a given point (e.g.,
reaction rates) while the conjugate voltages correspond to the covariant compon-
ents (e.g., affinities). Tellegen's theorem and the introduction of linear resis-
tances, which are constant over a differential range, lead to the typical
Riemmannian distance element. Schwarz's inequality translates into a parameter
which measures optimum dynamical efficiency and the elemental local volumes
(or higher dimensional measure of content) determined by the manifold coordinates
can be measured by looking at the efficiency of chemical energy conversion
along various paths which start at the same point on the energy hypersurface.
Because the distance element measured by using the port variables is equal to
sums of square of variables inside the resistive network (the power provided by
the inputs equals the sum of powers dissipated by the network resistances), the
network construction is equivalent to embedding the n-dimensional (non-orthogonal)
manifold in a higher dimensional (orthogonal) frame of reference of dimensionality
$d \geq n(n + 1)/2$. Vibrations in the transitions between two states in the chemical
manifold can be introduced by the additions of inductive and capacitive elements
which store energy as a function of a path parameter. The topological and metric
properties of the network lead to Lagrange's equations, geodesic equations and
stability requirements equivalent to a generalized Le Chatelier principle.

Abstract for Georgia Symposium on Chemical Applications of

of Topology and Graph Theory

Title: A LISP Program for the Manipulation of Chemical Graphs

Authors: Carl Trindle and Robert Givan, Department of Chemistry
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The representation and manipulation of chemical graphs is awkward in most familiar programming languages. LISP, the Esperanto of artificial intelligence research, makes possible a representation of chemical structural formulas which is much more nearly analogous to the chemist's use of such graphs. This is a considerable computational advantage as well as convenience for the user.

We will describe a "functional fragment" representation of structural formulas, applicable to any molecule, which will resolve a chemical graph into a list of fundamental fragments. Exploiting the property feature of LISP and the distance geometry algorithms of Crippen, we will recover Cartesian coordinates for each atom, suitable for input to molecular mechanics programs or _ab initio_ systems.

A method for recovering a chemical graph and Cartesian coordinates from an IUPAC name will be outlined as well.

E. C. HASS and P. J. PLATH

The Multi-Dimensional λ-Model. - A Graph Theoretical / Algebraic
Approach to Describe Mechanistic Aspects of Complex Chemical
Reactions.

Abstract

Based upon (1) the concept of the reaction lattice, generated
by graphs of the reaction, (2) a graph theoretical description
of bonding symbols, and (3) the model of a continuous
structural change of reactants into products by means of
reaction parameters (λ-model), correlation diagrams are
derived which lead to conclusions about the course of
chemical reactions. Using this formalism, closed analytical
formulae are derived for the Woodward-Hoffmann Rules for
concerted pericyclic reactions. Special emphasis is given to
multi-dimensional approaches in order to desribe mechanistic
aspects of complex organic reactions.

THE CLASSIFICATION OF CHEMICAL MECHANISMS FROM A GEOMETRIC VIEWPOINT

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ABSTRACT

A systematic method is introduced here for determining all mechanisms for a given chemical reaction, which are possible from a combinatorial viewpoint. Every mechanism is represented by a polyhedron in a real vector space. Every lower-dimensional face of such a polyhedron represents a submechanism, all of whose elementary steps advance in the same direction as those of the original mechanism. The vertices or zero-dimensional faces of the polyhedron correspond to the mechanisms, called <u>direct</u> <u>mechanisms</u>, which have minimal sets of steps. The fact that <u>this</u> polyhedron can be characterized by its set of vertices leads to the conclusion that every mechanism is reducible to a set of direct mechanisms connected in parallel. The method is illustrated by examples from chemistry which are sufficiently complex to be inaccessible without a mathematical approach such as this one.

MODELLING MOLECULAR COMPLEXITY

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ABSTRACT

A mathematical model of molecular complexity based on concepts from graph
theory and information theory has been developed (see JACS 1981, 3599, CC 1981,
818) and is being applied to analyze organic syntheses. Plots of complexity
vs. number of steps are used to estimate probable efficiency (JACS 1982, 5801).
Changes in complexity upon breaking bonds in a target help locate strategic
bonds in retrosynthetic analysis. Reactions can be rated according to the
increase in molecular complexity they produce. The principle of convergence is
clarified by considering symmetry in molecular graphs and synthesis graphs.

THE AUTOMORPHISM GROUPS OF SOME CHEMICAL GRAPHS

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In recent years many authors have used graphs for a variety of purposes in chemistry, in particular various "reaction graphs" have been studied in which the vertices represent chemical species and the edges chemical processes which interconvert these species. Some interest has been shown in determining the automorphism (symmetry) groups of reaction graphs. In general this is a hard problem, but many reaction graphs are highly symmetrical and since such graphs are comparatively few in number it is inevitable that some of those appearing in the chemical literature are ones which have already been discovered by mathematicians in totally different contexts.

We look at some examples of reaction graphs. In each case we start with a small graph B which has vertices labelled $1, 2, \ldots, n$ and we have some rearrangement rule which might consist of repositioning edges in the graph or of permuting the vertex labels. As we restrict our attention to degenerate rearrangements, the resulting graph is isomorphic to B but with the vertex labels redistributed. In the reaction graph Γ each vertex corresponds to a labelling and two vertices are joined by an edge if it is possible to interconvert the labellings by a single step application of the rearrangement rule. In most of our examples the automorphism group $\text{aut}\,\Gamma$ of Γ is the symmetric group S_n. We show that many reaction graphs are examples of what group theorists variously call suborbital, orbital or coloured graphs and this enables us to deduce that for such reaction graphs $\text{aut}\,\Gamma$ always contains S_n, though in some cases $\text{aut}\,\Gamma$ is much larger than S_n.

There is some information in the literature on suborbital graphs relevant to the question "when is a reaction graph connected?" and it is likely that there are other results which could be applied to reaction graphs.

[*]author presenting paper

GRAPHS, POLYMER MODELS, AND EXCLUDED VOLUME EFFECTS

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Simple graph-theoretical polymer models such as the random-walk
for chain polymers or the Cayley-Polya tree models for branched
alkanes do not account for volume exclusion—that is, the fact that
two pieces of a molecule do not occupy the same region of space at
the same time. Volume exclusion is accounted for in easily devised
corrected graph-theoretical models, such as self-avoiding walks on
a lattice for the case of chain polymers. However, as has long been
realized, these corrected models seem to be much more difficult to
deal with in an analytic fashion.

Here we discuss some generating function methods for both
uncorrected and corrected models. This entails fractal dimension
ideas, renormalization group approaches, and transfer matrix tech-
niques. Via such methods it seems that excluded volume models can be
attacked and useful properties deduced—in particular the mean spatial
extent of the model polymer conformations.

Finally we also note that graph-theoretic problems similar to
those occuring for models with volume exclusion also arise in a
variety of other statistical mechanical models and wavefunction cluster
expansions involving localized orbitals (or sites). Indeed volume
exclusion features seem to occur frequently in all areas of science;
for instance, branched structures seem most typically to exhibit such
features, although neither the usual graph-theoretic trees nor the
common branching process theory account for such features.

A VOLUME FUNCTION FOR WATER BASED ON A RANDOM LATTICE-SUBGRAPH MODEL

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ABSTRACT

It is shown how the following concept can be used to obtain a volume function for water.

If G is a connected r-regular labelled graph, let $RG(p)$ denote any subgraph of G having the same point set as G and line set defined by selecting or rejecting each of the lines of G with independent probability p or $q = 1 - p$, respectively. $RG(p)$ is called a <u>random subgraph of G</u> and is analyzed using the appropriate probabilistic considerations.

Here the graph G is taken to be homeomorphic to the ice lattice I and p, as a function of temperature, is associated with the hydrogen bonding probability of water molecules. Physical assumptions relating volume to bond and cycle formation lead to a volume function $V(p)$ which is qualitatively of the correct form. Additional assumptions, which match the bond percolation probabilities of certain subgraphs of $RI(p)$ with the phase transitions in water at $0^{\circ}C$ and $100^{\circ}C$, yield a good numerical fit of $V(p)$ to empirical data. With respect to the latter it is noted that the lack and/or wide discrepancy of physical and mathematical numerical results in the literature is a serious handicap in all studies of water.

This work is presented in support of the continued use of <u>random graph models</u> in physical applications.

THE BONDING TOPOLOGY OF POLYHEDRAL MOLECULES

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This paper summarizes the topology of the chemical bonding in molecules based on polyhedra having atoms at each vertex. In such molecules delocalized bonding occurs when there is a mismatch between the vertex degree of the polygon or polyhedron and the number of internal orbitals (normally but not necessarily 3) provided by the vertex atoms. This analysis leads naturally to the concepts of two-dimensional aromaticity in planar polygonal molecules such as benzene and three-dimensional aromaticity in deltahedral molecules such as certain carboranes and metal clusters. Elementary graph theoretical considerations provide a basis for the $2n + 2$ skeletal electrons normally observed in delocalized deltahedral molecules without tetrahedral chambers. Electron-rich polyhedral cluster systems have $2n + 2$ skeletal electrons and form polyhedra having one or more faces with four or more edges, which may be regarded as holes in the topological sense. Electron-poor polyhedral cluster systems have less than $2n + 2$ skeletal electrons and form deltahedra having one or more tetrahedral chambers. Puncture or excision of closed deltahedra to form electron-rich open polyhedra having one or more holes may be considered as opposite or dual to the capping of closed deltahedra to form electron-poor larger polyhedra having tetrahedral chambers. Elementary polyhedranes are hydrocarbons of the stoichiometry $(CH)_{2m}$ and are based on polyhedra with all vertices of degree 3 and a localized carbon-carbon single bond along each edge. The localized polyhedrane polyhedra are thus the duals of the delocalized deltahedra of carboranes and metal clusters.

TOPOLOGICAL PROPERTIES OF SULFUR NITROGEN COMPOUNDS

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ABSTRACT

The general question of the electronic structure of the binary compounds formed from nitrogen and sulfur will be discussed. This group of electron rich molecules and ions possess structures wherein it is not always evident which atoms are bonded to which other atoms or how this bonding occurs. The discussion and analysis will be based upon the results of semiempirical molecular orbital calculation (ref. 1) and utilize the concepts of localized molecular orbitals (ref. 2) and density functional analysis (ref. 3). The discussion will include the species S_2N_2, S_3N_2, $S_3N_3^-$, the isomers of S_4N_2, $S_4N_3^+$, $S_4N_4^{2+}$ and the molecule S_4N_4 (ref. 4).

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THE SHAPES OF MAIN GROUP CLUSTERS: A TOPOLOGICAL APPROACH TO SKELETAL ELECTRON COUNTING.

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ABSTRACT

A quantum topological approach, based on the topological properties of molecular charge densities is used to propose a symmetry heirarchy of molecular graphs. It is shown that the structures of a large number of cluster compounds may be predicted via a mapping of their molecular graphs onto a single polyhedron, the corresponding molecular graphs being constructed by a simple method of electron counting. The proposed model is exemplified through a detailed analysis of 5 through 8 atom clusters.

Typically, cyclo-octasulfur, S_8, has 48 valence electrons and, subtracting an exo-skeletal electron pair (analogous to those in the exo-skeletal BH bonds of the boranes), one is left with 16 skeletal electron pairs to hold together the cluster. It remains merely to find the highest symmetry polyhedron having 8 vertices, 16 edges and (from Euler's theorem) 10 faces. This is the square antiprism which indeed leads to the overall geometry of the S_8 molecule.
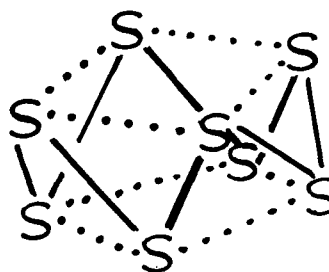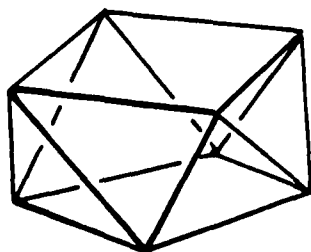
DYNAMICS OF RNA SECONDARY STRUCTURE FORMATION

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ABSTRACT

   We review the status of the RNA secondary structure problem and pose
a new approach based on simulating the dynamics of the folding process.
Constrained versus unconstrained models of folding are discussed as
are methods for detecting common features in the population of equilibrium
structures generated.

TOPOLOGICAL ASPECTS OF ENZYME-SUBSTRATE RECOGNITION

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ABSTRACT

Enzymes are compounds in the presence of which certain chemical reactions proceed at higher rates than would otherwise be the case. They are generally unchanged in amount and in their chemical properties after the reactions have occurred. Hence they belong to the class of catalysts; they are distinguished from other catalysts by the fact that they occur only as products of living organisms. A substance with which an enzyme reacts is called its substrate. All enzymes are functionally specific to varying degrees in their action on their substrates. An enzyme may act on one and only one substrate and the substrate molecule must be associated with the enzyme in a specific orientation. Thus there arises a problem of recognition in connection with the interaction of an enzyme with its substrate.

We describe a mathematical model for enzyme-substrate recognition. The foundations for this model were laid by L. Edelstein and R. Rosen. Their theory rests on the following assumptions:

(1) That substrates can be represented by continuous functions, which vanish outside some closed bounded region in $\mathbb{R}^3$, analogous to charge or mass distributions; i.e., substrates are represented by elements $F \in C(K)$, the space of all real-valued continuous functions on K, where K is a compact subset of $\mathbb{R}^3$ chosen to be large with respect to molecular dimensions.

(2) That recognition of the substrate corresponds to the evaluation of a linear functional on $C(K)$ -- or what is equivalent:

(2') That associated with a given enzyme is a function a in the dual space of $C(K)$, i.e., $a \in NBV(K)$, the space of all real-valued, normalized functions on K of bounded variation, and that recognition of a substrate F results from the evaluation of a Stieltjes integral of one form $\int F \, da$. (The equivalence of (2) and (2') is due to a theorem known as the Riesz Representation Theorem.)

The recognition problem can also be analysed in its functional context as a characteristic feature of a system which responds to specific inputs to
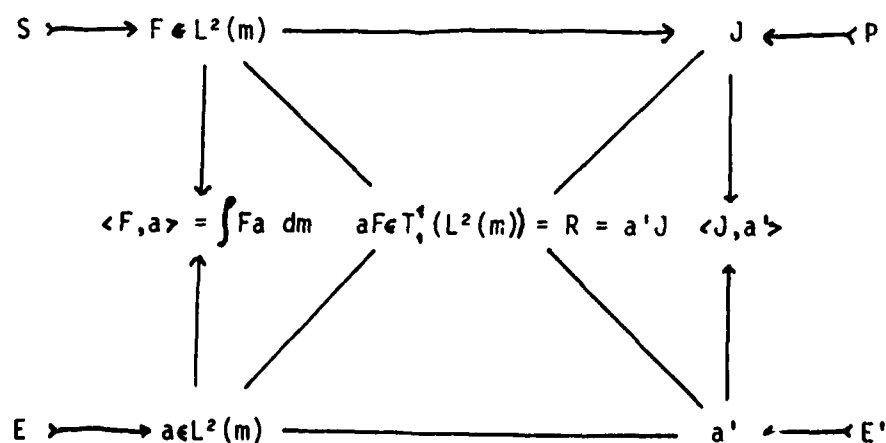
produce specific outputs. This point of view is explored by A.H.Louie, I.W. Richardson and S.Swaminathan[Journal of Theoretical Biology,94(1982) 77-93] . The mathematical formulation of the concept of system response and the associated description of a system in terms of response lead directly to a metric calculus providing a quantitative measure for discrimination. Moreover the metric structure inherent in this phenomenology allows one to determine the functional relationship between the physical features used by the system to recognize an input (e.g.,a substrate) and corresponding features possessed by the output(e.g.,the product).

The system is divided into distinct, interacting subsystems, indexed by a finite set $\{i=1,2,...,m\}$. The set of causes imposed upon the system(i.e.,the input) is given by various F_i belonging to some Hilbert space H. The system is characterized by a fixed set of constitutive parameters, a^i, which belong to the dual space H*. The system dynamics is phenomenologically described by a response tensor given by the dyadic $R = a^i F_i$. It is postulated that R is invariant with respect to transformations of the representation, i.e., with repect to a change of parameters. In particular, R has an invariant dual representation.

In the model for *enzyme-substrate recognition*, the a^i's represent enzymes and the F_i's represent substrates. The recognition process is given by the evaluation $a^i(F_i)$, while the enzyme-substrate complex is represented by the response tensor $a^i F_i$. The dual representation is the mathematical analogue of the enzyme-product complex. The mechanism of enzyme-substrate interaction can be represented as

$$E + S \rightleftharpoons ES \rightleftharpoons E'P \rightleftharpoons P + E'$$
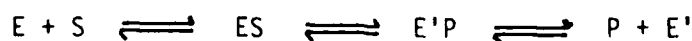
where ES is the enzyme-substrate complex, E'P is the ''enzyme-product''complex P is the product of interaction and E' the 'modified enzyme' from which the enzyme E can be recovered. The following diagram illustrates the model: